Application No.: 10/590,493 Amendment Under 37 C.F.R. 1.111

Art Unit: 1628 Docket No.: 032218A

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions of claims in the application.

1-12. (Cancelled)

13. (Currently Amended) A method of screening for a substance which improves <u>arteriosclerosis</u>

a vascular cell disorder which occurs due to the function of Rac protein, comprising:

adding a test substance to a first HUVEC culture which expresses a Rac fusion protein

comprising a HUVEC-expressing fluorescent protein, which contains a labelled Rac protein,

culturing a second HUVEC culture which expresses the Rac fusion protein comprising

the HUVEC-expressing fluorescent protein,

continuously culturing said first HUVEC culture and said second HUVEC culture for a

sufficient time for the Rac fusion protein to transfer into the nucleus, said first HUVEC culture

being continuously cultured in the presence of the test substance and said second HUVEC

culture being continuously cultured in the absence of the test substance,

measuring distribution of the amount of fluorescence in the transfer of the labelled Rae

protein into the nucleus of said first HUVEC culture and said second HUVEC culture, and

determining that the test substance is a substance which improves arteriosclerosis the

vascular cell disorder which occurs due to the function of Rac protein if the distribution of

fluorescence in the nucleus of said first HUVEC culture is greater than the distribution of

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fluorescence in the nucleus of said second HUVEC culture by a significant amount transfer of

the labelled Rac protein into the nucleus of said HUVEC is visually identified.

14-15. (Cancelled)

16. (Currently Amended) The screening method according to claim 13, or 14, wherein said first

HUVEC culture and said second HUVEC culture are cultured for measuring of the transfer of

the labelled Rac protein is performed 15 hours prior to said measuring distribution of the amount

of fluorescence in said first HUVEC culture and said second HUVEC culture after said test

substance is added to said HUVEC.

17-20. (Cancelled)

21. (Currently Amended) A method of screening for a substance which inhibits the function of

Rac protein, comprising:

adding a test substance to a first HUVEC culture which expresses a Rac fusion protein

comprising a HUVEC-expressing fluorescent protein, which contains a labelled Rac protein,

culturing a second HUVEC culture which expresses the Rac fusion protein comprising a

HUVEC-expressing fluorescent protein,

continuously culturing said first HUVEC culture and said second HUVEC culture for a

sufficient time for the Rac fusion protein to transfer into the nucleus, said first HUVEC culture

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being continuously cultured in the presence of the test substance and said second HUVEC

culture being continuously cultured in the absence of the test substance,

measuring distribution of the amount of fluorescence in the transfer of the labelled Rac

protein into the nucleus of said first HUVEC culture and said second HUVEC culture, and

determining that the test substance is a substance which inhibits the function of Rac

protein if the distribution of fluorescence in the nucleus of said first HUVEC culture is greater

than the distribution of fluorescence in the nucleus of said second HUVEC culture by a

significant amount transfer of the labelled Rac protein into the nucleus of said HUVEC is

visually identified

wherein the function of Rac is signal transmission mediated by angiotensin II, PDGF,

thrombin, endothelin and leukotriene B4 in vascular walls and promotion of activity of NADPH.

22-23. (Cancelled)

24. (Currently Amended) The screening method according to claim 21, or 22, wherein said first

HUVEC culture and said second HUVEC culture are cultured for measuring of the transfer of

the labelled Rac protein is performed 15 hours prior to said measuring distribution of the amount

of fluorescence in said first HUVEC culture and said second HUVEC culture after said test

substance is added to said HUVEC.

25. (Cancelled)

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